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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,646	01/11/2006	David Winn	063391-1106	7617

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EXAMINER	
HEARD, THOMAS SWEENEY	
ART UNIT	PAPER NUMBER
1654	
MAIL DATE	DELIVERY MODE
03/24/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,646	WINN, DAVID	
	Examiner	Art Unit	
	THOMAS S. HEARD	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-22,25-27 and 30* is/are rejected.

7)☒ Claim(s) *23, 24, 28, and 29* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/08/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/8/2009 has been entered.

The Applicants Amendments to the claims received on 9/8/2009 is acknowledged. The text of those sections of Title 35 U.S. Code not included in the action can be found in the prior office action. Rejections or objections not addressed in this office action with respect to the previous office action mailed 6/9/2009 are hereby withdrawn.

Claim(s) 20-30 are pending. Applicants have amended claim(s) cancelled prior claims 1-19 and introduced Claims 20-30 as their replacement. Claims 20-30 are hereby examined on the merits.

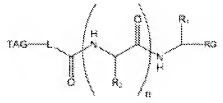
Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

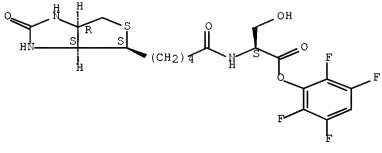
> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 20 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Wilbur et al, "*Biotin reagents for antibody pretargeting. 5. Additional studies of biotin conjugate design to provide biotinidase stability*," Bioconjugate Chemistry (2001), 12(4), 616-623.

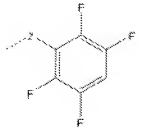
The instant invention is drawn to compounds of the following formula:



Wilbur et al discloses the compound (RN 295322-43-9 CAPLUS CN) N-[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-,yl]-1-oxopentyl]-, 2,3,5,6-tetrafluorophenyl ester L-Serine of the following formula:



In the instant case, the TAG is biotin, L is C_4 alkyl, n=0, R_1 is CH_2OH (Serine), RG is –



C(O)-LG, and LG is , where Z = O. The compound is compound **2g** of the reference article. The teaching of Wilbur et al therefore anticipates the instantly claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 20-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In Claims 20, the following are listed as detectable labels for TAG in Claim 20 on page 4 of the claims:

[F]luorescent moieties, electrochemical labels, biotin, digoxigenin, maltose, oligohistidine, 2,4-dinitrobenzene, phenylarsenate, ssDNA, dsDNA, a polypeptide, a metal chelate, a saccharide, dethiobiotin or structurally modified biotin-based reagents which bind to proteins of the avidin/streptavidin family; vicinal diols; maltose which binds to maltose binding protein, as well as any other sugar/sugar binding protein pair; a hapten to which an

antibody can be generated; a tag which binds to a transition metal such that the transition metal capture reagent may be used in the tbrm of a resin bound chelated transition metal; and glutathione.

It is unclear how electrochemical labels, biotin, digoxigenin, maltose, oligohistidine, 2,4-dinitrobenzene, phenylarsenate, ssDNA, dsDNA, a polypeptide, a metal chelate, a saccharide, dethiobiotin or structurally modified biotin-based reagents which bind to proteins of the avidin/streptavidin family; vicinal diols; maltose which binds to maltose binding protein, as well as any other sugar/sugar binding protein pair; a hapten to which an antibody can be generated; a tag which binds to a transition metal such that the transition metal capture reagent may be used in the form of a resin bound chelated transition metal; and glutathione, can be considered a detectable label. For example, a polypeptide is not a detectable label, but one can label a peptide with a detectable label.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 20-22, 25, and 26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed.

The factors considered in the Written Description requirement are:

(1) level of skill and knowledge in the art,

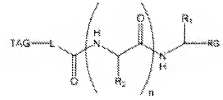
(2) partial structure,

(3) physical and/or chemical properties,

(4) functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and

(5) the method of making the claimed invention.

In the instant case, the claims are drawn to compounds of the following formula

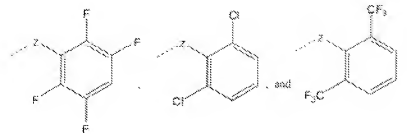


(1) Level of skill and knowledge in the art:

The level of skill to practice the art of the instantly claimed invention is high with regard to synthesis, isolation, physical and structural characterization for structure function relationships (SAR) in the bioassays the compounds are intended for.

(2) Partial structure: (3) Physical and/or chemical properties: and (4) Functional characteristics:

The partial structure is that of RG, where three options are disclosed



. The remaining variables are those of the Markush for TAG which are unrelated in chemical properties and function, such as ssDAN, polypeptide, biotin, or a fluorescent moiety, for example. The variance in R_1 and R_2, in addition to L, make the whole of the molecule beyond those of RG unrelated in structure and function.

(5) Method of making the claimed invention:

Chemical synthesis, solid phase or liquid phase.

As stated supra, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that Claim(s) 20 is a broad generic, with respect to all possible compounds encompassed by the claims. The possible structural variations are limitless to any class of compound where nearly every position is variant and does not produce a common core structure. As stated in the specification, the cysteine proteases are of great medical interest. Cysteine proteases in the papain family include mammalian enzymes such as cathepsins B and L, which are involved in cancer growth and metastasis, and cathepsin K, which is of importance for its involvement in bone degradation and parasites because they are essential for the parasite-host interaction and are therefore attractive targets of inhibition such as cruzipain from Trypanosoma cruzi, which causes Chagas' disease, and falcipain from Plasmodium falciparum, which causes malaria. Other cysteine proteases such as those belonging to the

legumain family, have been shown to play key roles in antigen presentation. Cysteine proteases of the caspase family are also of great interest as key mediators of apoptosis. Several cysteine proteases of pathogenic bacteria are virulence factors and cause severe problems for the host at infections, such as gingipains of Porhyromonas gingivalis, which is important in periodontitis, and streptopain from Streptococcus pyogenes. Cysteine proteases include, but are not limited to, papain, caspases, and several cathepsins such as cathepsins B, H, L, K, O, S, T, V, and X, ananain, papain, chymopapain, and fruit bromelain. The caspases are also cysteine hydrolases. Caspase-1 is a cysteine hydrolase that is also known by several other names including interleukin 1. β-converting enzyme, protease VII, protease A, interleukin 1β precursor protease, interleukin 1 converting enzyme, interleukin 1.beta.-converting endopeptidase, interleukin-1β. convertase, interleukin-1β. converting enzyme, interleukin-1β. precursor protease, prointerleukin 1β. protease, precursor interleukin-1β. converting enzyme, pro-interleukin 1βprotease.

Here, though the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds beyond compounds disclosed in the examples in the specification. There are numerous examples exemplified in Claims 22-30 and those examples share a very limited set of amino acids sequence for the variable of R_1 and R_2, and the fluorescent moieties for the TAG, or the one example of a non-fluorescent moiety of biotin. While having written description for the compounds listed in Claims 22-30, there is insufficient description of a common core structure, or a representative number of examples that would allow one of skill in the art to practice the invention as claimed. The variance for R_1 and R_2, with n = 4 allow for 20^4 peptide, which can then be attached to a poly peptide of any length (TAG). Different also is the absence of R1 when n=0, which makes a complete

different set of compounds unrelated in structure. The variance in each position is far too broad in relation to what was actually made, and as such the limited numbers of samples do not inform the skilled artisan what can be made that correlates to a cysteine protease ligand.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.")

Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

New Matter

Claims 20 and 30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

The response filed 9/8//2009 has introduced NEW MATTER into the claims. Newly added/amended claim 20 recites "*R_1 and/or R_2 is -CH_2-CH_2-CH_2-, such that R_1 and/or R_2, along with the -NH- adjacent thereto, forms a pyrrolidine ring,*" or, in Claim 20 the change in n from 1-4 to 0 t-4, appears to be a new range that does not have support, or in Claim 30, the limitation (wherein Z at each occurrence refers to -C(O)-O-CH:-phenyl), and neither of these newly amended claims appear to have support, either explicit or implicit. . The

response did not point out where support for newly added/amended Claim(s) 20 or 30 could be found in the originally filed disclosure. Although the PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims, when filing an amendment an applicant should show support in the original disclosure for new or amended claims. See MPEP 714.02 and 2163.06 ("Applicant should therefore specifically point out the support for any amendments made to the disclosure."). Instant Claim(s) 20 and 30 now recites limitations which were not clearly disclosed in the specification as filed, and now change the scope of the instant disclosure as filed, and do not have implicit or explicit support. The new limitation of Claim 20 is not supported in the specification and the term pyrrolidine does not appear to be even used in the specification. Further, Z never appears to be an option for modifying the compounds listed in Claims 30. Such limitations recited in newly added claims, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C 112. Applicant is required to provide sufficient written support for the limitations recited in present claims in the specification or claims, as-filed, or remove these limitations from the claims in response to this Office Action.

Claim Objections

Claims 20, 21, 25 are objected to because of the following informalities: In Claim 20, the variable for the side chains of the naturally occurring amino acids, such as –H. $-CH_3$, etc… would be better understood as H, CH_3, etc…without the line dran to the atom. This is already present in the structure and would be understood that R_1 is H and not -H, or CH_3 and not $-CH_3$.

Appropriate correction is required.

Conclusion

Claims 23, 24, 27, and 29 appear free of the prior art. The species in claim 30 also appear free of the prior art. No other claims are allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Prior art contained in the reference of record can be applied in the next office action.

Applicant should specifically point out the support for any amendments made to the disclosure, including the claims (MPEP 714.02 and 2163.06). Due to the procedure outlined in MPEP § 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 U.S.C. § 102 or 35 U.S.C. § 103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending applications that set forth similar subject matter to the present claims. A copy of such copending claims is requested in response to this Office action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thomas S. Heard whose telephone number is (571) 272-2064. The examiner can normally be reached on 9:00 a.m. to 6:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Anish Gupta/
Primary Examiner, Art Unit 1654

/Thomas S Heard/
Examiner, Art Unit 1654